# CANCER DRUG PHARMACOLOGY TABLE

## Cytotoxic Chemotherapy

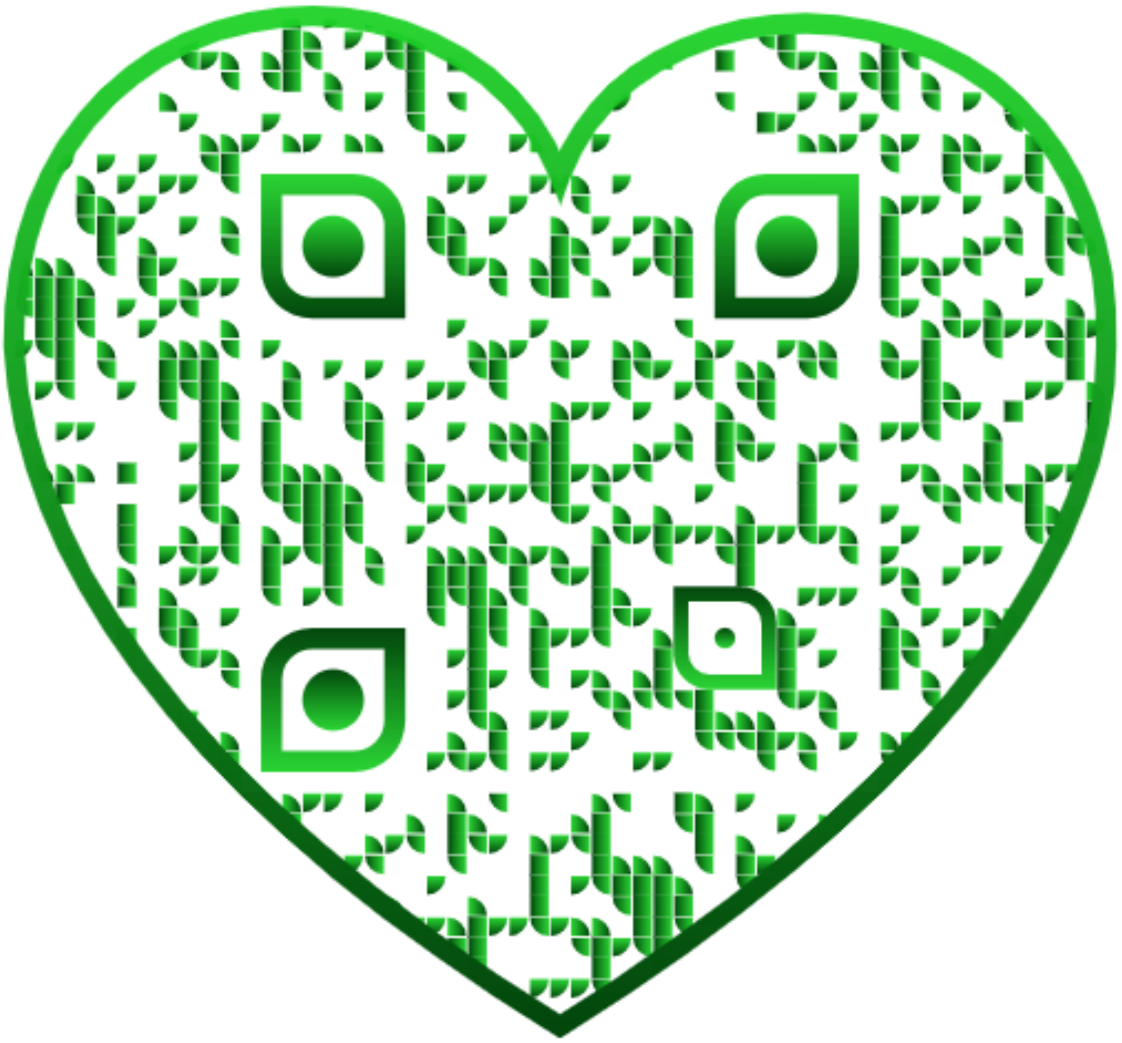
Drugs are classified according to the BC Cancer Drug Manual Monographs, unless otherwise specified (see asterisks). Subclassifications are in brackets where applicable.

**Alkylating Agents** have reactive groups (usually alkyl) that attach to DNA or RNA, leading to interruption in synthesis of DNA, RNA, or proteins.

- bendamustine (nitrogen mustard)
- busulfan (alkyl sulfonate)
- carboplatin (platinum)
- carmustine (nitrosurea)
- chlorambucil (nitrogen mustard)
- cisplatin (platinum)
- cyclophosphamide (nitrogen mustard)
- dacarbazine (triazine)
- estramustine (nitrogen mustard with 17-beta-estradiol)
- hydroxyurea
- ifosfamide (nitrogen mustard)
- lomustine (nitrosurea)
- mechlorethamine (nitrogen mustard)
- melphalan (nitrogen mustard)
- oxaliplatin (platinum)
- procarbazine (triazine)
- streptozocin (nitrosurea)
- temozolomide (triazine)
- thiotepa (aziridine)
- treosulfan

**Antimetabolites** are structural analogues of naturally occurring molecules required for DNA and RNA synthesis. When substituted for the natural body substances, they disrupt DNA and RNA synthesis.

- azacitidine (pyrimidine analogue)
- capecitabine (pyrimidine analogue)
- cladribine (adenosine analogue)
- cytarabine (pyrimidine analogue)
- fludarabine (purine analogue)
- fluorouracil (pyrimidine analogue)
- gemcitabine (pyrimidine analogue)
- mercaptopurine (purine analogue)
- methotrexate (folate analogue)
- pralatrexate (folate analogue)
- pemetrexed (folate analogue)
- pentostatin (purine analogue)
- raltitrexed (folate analogue)
- thioguanine (purine analogue)
- trifluridine-tipiracil (pyrimidine analogue/thymidine phosphorylase inhibitor)



**Antimicrotubule Agents (Mitotic Inhibitors)** inhibit cell mitosis by interfering with microtubule formation or function.

- cabazitaxel (taxane)
- docetaxel (taxane)
- eribulin
- ixabepilone
- paclitaxel (regular and nanoparticle, albumin-bound) (taxane)
- vinblastine (vinca alkaloid)
- vincristine (vinca alkaloid)
- vinorelbine (vinca alkaloid)

**Miscellaneous Antineoplastics** - Refer to BC Cancer monographs for pharmacology.

- arsenic trioxide
- asparaginase
- belzutifan
- bleomycin
- belinostat
- crisantaspase recombinant
- dactinomycin
- decitabine - cedazuridine
- iniparib
- lurbinectedin
- mitomycin
- mitotane
- pegaspargase
- porfimer
- romidepsin
- vorinostat

**Topoisomerase Inhibitors (I and II)** cause DNA strand breaks by disrupting the function of topoisomerase enzymes, which are responsible for regulating the 3-D structure of DNA.

Topoisomerase I

- irinotecan
- topotecan

Topoisomerase II

- amsacrine
- anthracyclines
  - daunorubicin
  - doxorubicin (regular and pegylated liposomal)
  - epirubicin
  - idarubicin
- etoposide
- mitoxantrone
- teniposide

## Hormonal Therapies

**Antiestrogens** oppose the effects of estrogen.

- tamoxifen – partial estrogen antagonist (antagonist on breast tissue, agonist on endometrium, bone and lipids)
- fulvestrant – full estrogen antagonist (no agonist activity)

**Antiandrogens** opposes the effects of androgens.

- apalutamide

**Aromatase Inhibitors (AIs**) prevent the final step in the conversion of androgens to estrogens in peripheral tissues.

- anastrozole
- exemestane
- letrozole

**Luteinizing Hormone Releasing Hormone (LHRH) Agonists** (also known as gonadotropin releasing hormone analogues) initially stimulate the release of luteinizing hormone, which leads to an increase in sex hormones

- bicalutamide
- darolutamide
- enzalutamide – more affinity for androgen receptors and Plus inhibits more steps in the androgen inhibition than other agents in this class
- flutamide
- nilutamide

**Androgen Biosynthesis Inhibitors**

- abiraterone - selectively inhibits the enzyme (CYP17) that converts pregnenolone and progesterone into testosterone precursors.

**Androgens**

- testosterone **-** The exact mode of action for androgen therapy in breast cancer is unclear.

**Corticosteroids** are thought to act via apoptosis induction.

- dexamethasone
- prednisone

**Somatostatin Analogues** inhibit exocrine and endocrine secretion of hormones, which is useful for hormone-secreting tumours (e.g., neuroendocrine). Additional mechanisms include modulation of biliary/GI motility and apoptosis inductions.

- lanreotide
- octreotide

**Thyrotropin Stimulating Hormone Agonist** is a recombinant thyrotropin used for serum thyroglobulin testing in thyroid cancer.

(testosterone, estradiol). Chronic use leads to down-regulation of the LHRH receptors, leading to decreased testosterone in men and estrogen in women.

- buserelin
- goserelin
- leuprolide

**Luteinizing Hormone Releasing Hormone (LHRH) Antagonist** (also known as gonadotropin releasing hormone antagonist) reduce the release of luteinizing hormone, follicle-stimulating hormone, and consequently testosterone by the testes.

- degarelix

**Progestins** suppress the release of luteinizing hormone from the pituitary gland and subsequently decrease estrogen levels. Additional mechanisms include binding to progesterone, glucocorticoid, and androgen receptors, resulting in decreased number of estrogen receptors and decreased estrogen and progesterone levels peripherally in target tissues.

- medroxyprogesterone
- megestrol

**Prolactin Lowering Agents** are dopamine antagonists that decrease hormone production and the size of prolactin-dependent pituitary adenomas by inhibiting the release and synthesis of prolactin from the anterior pituitary.

- bromocriptine
- cabergoline
- quinagolide

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| • thyrotropin alpha | |

## Immunotherapies

**Cytokines** are proteins that are involved in the cell signaling that leads to immune responses at sites of inflammation, infection, and trauma. They induce various cellular responses, such as suppression of cell proliferation and augmentation of the cytotoxicity of lymphocytes.

- aldesleukin
- interferon
- peginterferon

**Vaccine Therapy**

- bacillus calmette-guerin (BCG)
  - a live, attenuated bacteria (Mycobacterium bovis) that exerts a variety of antitumour actions, including induction of a local granulomatous reaction, activation of histiocytes, and other direct and indirect stimulation of immune responses. The result is a local inflammatory response that destroys tumour cells.

**Immunomodulatory Drugs (IMIDs)** have multiple mechanisms of action, including inhibition of proliferation of certain hematopoietic tumour cells, enhancing numbers and activity of T, NK, and NK T cells, and inhibition of angiogenesis.

- lenalidomide
- pomalidomide
- thalidomide

**Differentiating Agents** are vitamin A derivatives. Their proposed mechanism of action is to overcome impaired cellular differentiation.

- acitretin
- alitretinoin
- bexarotene
- tretinoin

**Other Immunotherapies**

- imiquimod – TLR7 agonist
- Monoclonal antibodies could also be considered immunotherapies, particularly those that inhibit CTLA-4, PD-1 or PD-L1 (Checkpoint Inhibitors), or IL-6. They are covered on the pages that follow.

## Targeted Therapies

Targeted therapies target receptors, ligands, or intracellular molecules involved in the signal transduction of cancer cells. The following table is a listing of targeted therapies with the target(s) listed in brackets. See the following page for more information on targets. Note that the relative affinity

to particular targets is not always clear for each agent, and may differ when used in different indications. Some of the available literature refer to drugs by their target, such as EGFR-inhibitors or multikinase inhibitors for oral drugs with multiple targets (e.g., pazopanib,sorafenib, sunitinib).

abemaciclib (CDK 4/6)
acalabrutinib (BTK)
afatinib (EGFR, HER2, HER4)
AGS-16C3F (MMAF) (antibody conjugated with cytotoxic)
alectinib (ALK)
alemtuzumab (CD52)
amivantamab (low-fucose IgG1 bispecific antibody binding to EGFR and MET)
asciminib (ABL-TKI myristoyl pocket (STAMP)
atezolizumab (PD-L1)
avelumab (PD-L1)
axitinib (VEGFR 1, 2, & 3)
bevacizumab (VEGF)
belantamab mafodotin (IgG1) (antibody conjugated with cytotoxic)
binimetinib (MEK)
blinatumomab (CD3 & CD19)
bortezomib (26S proteosome)
bosutinib (BCR-ABL TKI)
brentuximab vedotin (CD30) (antibody conjugated with cytotoxic)
brigatininb (ALK) (ROS1) (EGFR) (IGF) (FLT3)
cabozantinib (MET, VEGF, FLT3)
carfilzomib (26S proteosome)
carotuximab (aka TRC105) (CD105)
cemiplimab (PD-1)
durvalumab (PD-L1)
elranatamab (IgG2 bispecific antibody against BCMA and CD3)
encorafenib (BRAF V600E, V600D,V600K, wt-BRAF, CRAF, JNK1, 2, 3, LIMK1, 2, MEK4 and STK3)
enfortumab vedotin (Nectin-4)(antibody drug conjugate)
entrectinib (NTRK gene fusion)
epcoritamab (bispecific antibody) (CD3 on T cells & CD20 on B-cell malignant cells)
erlotinib (EGFR)
everolimus (MTOR)
fedratinib (JAK2, FLT3)
gefitinib (EGFR)
gemtuzumab ozogamicin (CD33) (antibody conjugated with cytotoxic)
gilteritinib (FLT-3)
ibrutinib (BTK)
idelalisib (PI3Kδ)
imatinib (BCR-ABL, PDGF, c-KIT)
inotuzumab ozogamicin (CD22) (antibody conjugated with cytotoxic)
ipilumumab (CTLA-4)
Isatuximab (IgG1 antibody) (CD38)
lapatinib (EGFR, HER2)
larotrectinib (tropomyosin receptor kinase) (NTRK gene fusion)
pembrolizumab (PD-1)
pertuzumab (HER2)
polatuzumab vedotin (CD79b) (antibody conjugated with cytotoxic)
ponatinib (BCR-ABL TKI)
pralsetinib (RET tyrosine kinase inhibitor)
ramucirumab (VEGFR2 and VEGF A, C, and D)
regorafenib (VEGFR-1, -2, & -3, TIE2, KIT, RET RAF-1, BRAF, BRAV600E, PDGFR, FGFR)
ribociclib (CDK 4/6)
ripretinib (kinases KIT and PDGFRA)
rituximab (CD20)
ruxolitinib (JAK 1 & 2)
sacituzumab govitecan (IgG1.k antibody conjugated with cytotoxic)
selpercatinib (RET fusion positive)
selinexor (SINE)
siltuximab (IL-6)
sonidegib (Hh)
sorafinib (c-Raf,b-Raf, V600E,b-Raf,KIT,FLT-3, VEGFR -2, -3 & -beta)
sunitinib (VEGFR 1, 2, & 3, PDGFR α & β), KIT, FLT-3, CSF-1R, RET)
tebentafusp (fusion protein on CD3)
teclistamab (bispecific antibody targets CD3 on T and B cell maturation antigen (BCMA)
temsirolimus (MTOR)
tislelizumab (IgG4) (PD-1)

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| ceritinib (ALK)<br>cetuximab (EGFR)<br>cobimetinib (MEK)<br>crizotinib (ALK, HGFR, C-Met, ROS1)<br>dabrafenib (BRAF)<br>dacomitinib (EGFR)<br>daratumumab (CD38)<br>dasatinib (BCR-ABL, LYN, HCK, c-kit, EPH, PDGFβ)<br>denosumab (RANKL)<br>dinutuximab (GD2) | lenvatinib ( VEGFR, FGFR, PDGFRα, KIT, RET)<br>lorlatinib (ALK & ROS1)<br>midostaurin (FLT-3, KIT, PDGFR)<br>mogamulizumab (IgG1.k antibody)<br>nilotinib (BCR-ABL, c-KIT, PDGFR)<br>niraparib (PARP-1, PARP-2)<br>nivolumab (PD-1)<br>obinutuzumab (CD20)<br>ofatumumab (CD20)<br>olaparib (PARP-1, PARP-2, PARP-3)<br>olaratumab (PDGFR α)<br>osimertinib (EGFR)<br>panitumumab (EGFR)<br>palbociclib (CDK 4/6)<br>pazopanib (VEGFR 1, 2, 3, c-KIT, PDGFR-α,-β, c-KIT,FGFR-1 and -3, IL-2, and c-Fms) | tocilizumab (IL-6)<br>trametinib (MEK 1 & 2)<br>trastuzumab (HER2)<br>trastuzumab emtansine (HER2) (antibody conjugated with cytotoxic)<br>trastuzumab deruxtecan (HER2) (antibody conjugated with cytotoxic)<br>tucatinib (HER2)<br>vandetanib (VEGFR-2, EGFR, RET)<br>vemurafenib (BRAF)<br>venetoclax (BCL-2)<br>vismodegib (Hh)<br>zanubrutinib (BTK) |

The last letters in the drug names in the table provide information about the classification of the drug:

- mab = monoclonal antibody
- zomib = proteasome inhibitor
- nib = kinase inhibitors
- olimus = MTOR inhibitor

## Target Listing

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| ALK | Anaplastic Lymphoma Kinase | Translocations in this gene lead to oncogenic fusion proteins that play a role in many cancers, including non-small-cell lung cancer. |
| BCL-2 | B-cell chronic lymphoma 2 | BCL-2 is an anti-apoptotic protein |
| BCMA | B Cell maturation antigen | |

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| BCR-ABL | Breakpoint Cluster Region – Abelson Leukemia | This is the fusion protein created by the abnormal Philadelphia chromosome, which characterizes chronic myeloid leukemia. |
| BRAF | BRAF Serine-Threonine Kinase | BRAF plays a role in cell growth, differentiation, and survival. |
| BTK | Bruton's Tyrosine Kinase | BTK is involved in tumour proliferation, migration, and survival. |
| CD | Cluster Of Differentiation Antigens | CDs are a group of antigens present on the surface of all cells in different combinations, which makes them useful for classifying cells.<br>• CD3 is found on T cells<br>• CD19 is found on B cells<br>• CD20 is found on B cells<br>• CD30 is expressed on Hodgkin's Lymphoma and anaplastic large cell lymphoma cells (16)<br>• CD38 is highly expressed on myeloma cells, but is expressed at low levels on normal lymphoid and myeloid cells<br>• CD52 is found on the surface of B and T lymphocytes, most monocytes, macrophages and NK cells, and certain granulocytes<br>• CD105 (endoglin) expression is required for vascular endothelial cell proliferation. Targeting CD105 is a novel approach to inhibiting angiogenesis in cancer cells. |
| CDK 4/6 | Cyclin-dependent kinases | CDK4/6 form complexes with cyclin D to promote phosphorylation of retinoblastoma (Rb) protein, which allows cell cycle progression. |
| C-Kit | Stem Cell Factor Receptor | C-Kit is involved in oncogenesis. 95% of GIST cells have c-Kit mutations. |
| CRAF | Cellular (RAF) Rapidly Accelerated Fibrosarcoma | Plays a critical role in mediating the cellular effects of growth factor signals. |
| CTLA-4 | Cytotoxic T Lymphocyte-Associated Antigen 4 | CTLA-4 acts as an immune response checkpoint by switching off T-cells. Agents that target CTLA-4 are referred to as Checkpoint Inhibitors. |
| EGFR | Epidermal Growth Factor Receptor (also referred to as HER1) | EGFR is involved in cancer cell proliferation, blocking apoptosis, mobilizing cells to promote metastasis, and angiogeneisis. |
| EPH | Ephrin Receptor | EPH may be involved in the development of resistance to imatinib. |
| FGFR | Fibroblast Growth Factor Receptor | FGFR contributes to the maintenance of the tumour microenvironment. |

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| FLT3 | FMS-Like Tyrosine Kinase 3 | Like other tyrosine kinase inhibitors, FLT3 competes for the ATP binding site in the active domain of the kinase, which inhibits the ability of the protein to be phosphorylated, and subsequently decreases activity of the protein. |
| GD2 | Disialoganglioside | GD2 is a surface antigen found on the surface of neuroblastoma cells. |
| HER | Human Epidermal Growth Factor (also known as EGFR) | HER2 is overexpressed in about 20% of breast cancers, which leads to increased cell proliferation, cancer spread, and apoptosis inhibition. |
| Hh | Hedgehog Pathway | This pathway is normally dormant in adult tissues, but basal cell carcinomas have gene mutations that activate the Hh pathway, which promotes tumour survival and cancer spread. |
| IGF (1 &2) | Insulin-like growth factor | Produce insulin-like actions in some tissues, they are far less vvv than insulin in decreasing blood glucose concentrations. Their fundamental action is to stimulate growth. |
| Ig | Immunoglobulins | Are proteins produced by B lymphocytes and plasma cells. Each subclass possesses a unique manner of antigen binding and immune complex formation. Immoglobulins are also known as antibodies. |
| IgG (1,2,3,4) | Immunoglobulin G | IgG (1-4) provides the majority of antibody-based immunity and is the main type of antibody in blood and extracellular fluid. |
| JAK | Janus Associated kinase | JAK mediates the signaling pathway of cytokines and growth factors for hematopoiesis and immune function. |
| JNK | c-Jun N-terminal kinase | (Also known as stress-activated protein kinase, SAPK) is one of the 3 major members of the mitogen-activated protein kinase (MAPK) superfamily. |
| LYN | Lck/Yes novel tyrosine kinase | LYN is involved in BCR-ABL signaling |
| LIMK | Lim Kinase | Are actin-binding kinases that phosphorylate members of the ADF/cofilin family of actin binding and filament severing proteins. |
| MEK | Mitogen-Activated Extracellular Signal-Regulated Kinase | MEK1 and MEK2 are involved in cell growth, differentiation, inflammation, and apoptosis. |
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| MTOR | Mammalian Target of Rapamycin | Inhibit cell proliferation and angiogenesis. |
| Nectin-4 | Adhesion protein on surface of cells | (Nectin Cell Adhesion Molecule 4) is a Protein Coding gene. In the antibody–drug conjugate (ADC), human anti-nectin-4 antibody is linked to the cytotoxic microtubule-disrupting agent monomethyl auristatin E |

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| NTRK | Neurotrophic tyrosine kinase inhibitor | NTRK (NTRK1, NTRK2, NTRK3) gene fusions are oncogenic drivers of various tumour types. TRK proteins are receptor kinases that help regulate cell signaling and function in healthy tissues. |
| PARP | poly (ADP-ribose) polymerase | Binding to PARP inhibits single stranded DNA base excision repair and creates PARP-DNA complexes that lead to double-stranded DNA breaks, ultimately causing cell death. |
| PD-1<br>PD-L1 | Programmed Death Receptor 1 and Programmed Death Receptor Ligand 1 | PD-1 receptors are located on T-cells. When ligands bind to PD-1 receptors, they switch off T-cells, which fight cancer. Agents that target PD-1 are referred to Checkpoint Inhibitors. |
| PDGF | Platelet-Derived Growth Factor | PDGF contributes to maintenance of tumour microenvironments. |
| PI3Kδ | Phosphoinositide 3-kinase | Active in the signalling pathways of B-cell malignancies |
| Proteosome | Proteosome | Proteosomes degrade cellular proteins targeted for destruction. Inhibition of the proteasome results in cell cycle arrest and apoptosis. |
| RAF | Rapidly Accelerated Fibrosarcoma (see BRAF and CRAF) | RAF kinases are a family of three serine/threonine-specific protein kinases from the TKL (Tyrosine-kinase-like) group of kinases. RAF kinases participate in the RAS-RAF-MEK-ERK signal transduction cascade, also referred to as the mitogen-activated protein kinase (MAPK) cascade. |
| RANKL | Receptor Activator Of Nuclear Factor Kappa-B Ligand | RANKL activates osteoclasts, leading to bone resorption. |
| RET | Rearranged during transfection | RET is involved in oncogenesis (proto-oncogene which encodes a receptor tyrosine kinase for members of the glial cell line-derived neurotrophic factor (GDNF) family of extracellular signalling molecules. |
| ROS1 | c-ros oncogene1 | ROS is a proto-oncogene which may mutate to become an oncogene. |
| SINE | Selective inhibitor of Nuclear Export | SINE target XPO1, arrest tumor suppressor proteins in the nucleus and induce apoptosis |
| STAMP | Specifically Targeting the ABL Myristoyl Pocket | Wild-type ABL has a myristoylated N-terminus which binds to an allosteric site, but the ABL fusion protein does not have the myristoylated domain. In wild-type ABL, when myristoylated N-terminus binds to the allosteric site, the kinase has reduced activity. The mutant fusion protein does not have the myristoylated N-terminus domain and is not subject to this form of regulation, and the fusion protein is constitutively active. |
| STK3 | serine/threonine-protein kinase 3 | STK receptors play a role in the regulation of cell proliferation, programmed cell death (apoptosis), cell differentiation, and embryonic development. |

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| TLR7 | Toll-like receptor 7 | TLR7 stimulates innate and cell-mediated immunity to induce antitumour effects, including the increased production of inflammatory cytokines, such as tumour necrosis factor-α (TNFα), interferon-α, and interleukin-12. |
| VEGF<br>VEGFR | Vascular Endothelial Growth Factor and Vascular Endothelial Growth Factor Receptor | VEGF and VEGFR are involved in the development of a tumour blood supply (angiogenesis). |

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